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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,444	12/20/2005	Yuso Tomohira	Q92094	6406

23373 7590 05/21/2010

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EXAMINER	
SUTTON, DARRYL C	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
05/21/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/561,444	TOMOHIRA, YUSO	
	Examiner	Art Unit	
	DARRYL C. SUTTON	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *1-20,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/20/2005, 03/06/2006 & 12/15/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 21- 30, in the reply filed on 04/23/2010 is acknowledged. Claims 1-20, 31 and 32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

IDS

The information disclosure statement filed 12/20/2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it lists duplicate citations that have been considered. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-25 and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akiyama et al. (US 5,593690) in view of Bartholomaeus et al. (US 2002/0176888).

Akiyama et al. teach a matrix preparation produce by dispersing a pharmaceutically active ingredient into a matrix which is solid at ambient temperature and comprised of a fatty acid ester of a polyglycerol. The preparation has stable release-controlling ability, can be processed to fine granules, tablets or capsules and contributes to reduce the administration times of the active ingredient and side effects of the ingredient (Abstract). The present inventors have found that when an active ingredient is dispersed into a matrix being solid at ambient temperature and consisting of a fatty acid ester of a polyglycerol, which has not been employed in conventional matrix preparations, an ideal controlled release matrix preparation, particularly fine granules, can be unexpectedly prepared; and that the method uses no harmful solvents and can be easily adjusted in dissolution rate (column 1, lines 34-47, column 7, lines

36-41). The fatty acid ester of a polyglycerol in this invention is an ester formed by the combination of a polyglycerol with a fatty acid. As the polyglycerol, there can be used those represented by the formula I, where n is preferably 2-10. Specific examples include triglycerols. As the fatty acid, there are used behenic acid. As the fatty acid esters of polyglycerols, there are used monoesters or polyesters, i.e. diesters, triesters, etc., from the polyglycerols and fatty acids mentioned above (column 2, lines 35-66). The polyglycerol esters have a molecular weight of 200 to 5,000 and an HLB, hydrophilic-lipophilic balance, of 1 to 22. The fatty acid ester of polyglycerols can suitably be selected depending upon the type of active ingredients utilized, for example those being capable of melting by warming active ingredients in proportions of 0.00001 to 5 g/mL (column 2, line 66 - column 3, line 7). These fatty acid esters of polyglycerols are used in such quantities as correspond to about 0.001 to 50 times the weight of the active ingredient (column 3, lines 41-45). The matrixes containing fatty acid esters of polyglycerols can be incorporated with lipids, such as glycerides, i.e. glycerol fatty acid esters, in amounts that correspond to 0.01 to 100 times the weight of the active ingredient to assist in regulating the dissolution rate of drugs (column 3, line 53 - column 4, line 18). The matrixes suitably incorporate additives being generally employed in the production of fine granules, including as binding agents such as starch, sucrose, gelatin, powdered gum, sodium carboxymethylcellulose and polyvinylpyrrolidone (column 4, lines 9-18). Active ingredients include theophylline in amounts of 0.005 to 75% of the granule (column 5, lines 26-31 and lines 55-59). The stable, controlled release matrix preparations, particularly granules and fine granules can be obtained by melting by

warming at 40° to 150°C, a fatty acid ester of a polyglycerol alone or in conjunction with the above mentioned additives, adding to the melted substance an active ingredient in suitable amounts to produce a dispersion followed by cooling and bring a matrix (column 6, lines 8-20). Granulation under cooling is particularly preferred for producing fine granules, such as spray cooling through spray chilling (column 6, lines 38-41). Fine granules can be coated with a coating agent by a per se known method. Coating agent, such as ethylcellulose, waxes and talc can be used alone or in combination (column 6, lines 49-65). The coating of fine granules is preferably carried out at a temperature of 25° to 70°C (column 7, lines 3-4). The granules and fine granules possess extremely stable controlled release ability being free from variation and hardly show any change in drug release after storage for a prolonged period of time. The present preparations do not produce any static charge (column 7, line 42).

Akiyama et al. do not teach fusion-coating, the hydroxyl value of the matrix materials or triglycerol behenic acid half ester.

Bartholomaeus et al. teach controlled release dosage formulations in the form of granules (Abstract and [0043]). Retarding coatings is applied to the dosage formulation by fusion processes or powder application [0040]. Wax coatings can be applied by fusion-coating in a fluidized bed and cooling after coating until completely hardened at temperatures below the relevant fusion temperature [0057]. Fusion coating is a method of applying a coating powder on a substrate in which dry, finely divided, free flowing heat fusible powders are deposited on the substrate and then fused and cured with

heating, i.e. after coating the coated substrate is subjected to a heat treatment, to form continuous or protective films.[1]

Bartholomaeus et al. do not teach a matrix base material that has a hydroxyl value of 60 or greater and contains a polyglycerol fatty acid ester.

At the time of the invention, it would have been obvious to modify the methods of Akiyama et al. by utilizing the method of fusion coating of Bartholomaeus et al. for the coating step since it is an art recognized method of coating a granule to provide controlled release of a pharmaceutical, and the invention of Akiyama et al. is controlled release formulation.

At the time of the invention, it would have been obvious to use a fatty acid ester of a polyglycerol, in the form of a triglycerol diester of behenic acid, i.e. a polyglycerol fatty acid half ester, since the fatty acid esters of polyglycerols disclosed by Akiyama et al. include a triglycerol diester of behenic acid, i.e. a polyester compound, i.e. a compound comprising more than one ester, comprised of a triglycerol and of fatty acids, i.e. behenic acid, to create the ester linkages.

Since the granules suggested by combining Akiyama et al. and Bartholomaeus et al. are comprised of substantially the same components as the instant invention, the base material, i.e. triglycerol diester of behenic acid, would reasonably be expected to possess the same hydroxyl value.

In regard to claim 23, the prior art does not teach the specific temperature of the fusion coating. The prior art does not disclose the exact claimed values, but does

[1] Muthiah, US 6,537,671, column 1, lines 30-35.

overlap: in such instances even a slight overlap in range establishes a *prima facie* case of obviousness. In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003). Akiyama et al. teach that the coating is done at a temperature from 25° to 70°C, and the fatty acid ester of a polyglycerol matrix base material melts at a temperature from 40° to 150°C, versus fusion coating performed at a temperature in the vicinity of the melting point of the matrix base material.

In regard to claim 27, the continuity and protective activity of the fusion coating and subsequent release of the active ingredient can be optimized through routine experimentation by varying the temperature of the curing step in the fusion coating process with the temperature of the coating process, i.e. 25° to 70°C as a reference point. (The prior art teaches that in the process of fusion coating, protective coatings and continuity of the coatings is produced by heat treatments; and that fusion coating is used for controlled release. It seems obvious from these teachings that the control release is dependent on the coating which is affected by curing, i.e. a heat treatment).

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Akiyama et al. and Bartholomaeus et al. as applied to claims 21-24 and 28-30 above, and further in view of Kojima et al. (J. of Controlled Release, 2002).

Akiyama et al. and Bartholomaeus et al. are discussed *supra*.

Akiyama et al. and Bartholomaeus et al. do not teach subjecting the core particles to a heat treatment before fusion coating.

Kojima et al. teach methods of developing controlled release matrix pellets by annealing with micronized water-insoluble polymers (Abstract). Spray chilling by using a polyglycerol ester of a fatty acid is an alternative method of manufacturing matrix controlled release pellets (page 336, 1st column, 1st paragraph). Ethylcellulose was used as the water insoluble polymer and theophylline was used as the pharmaceutical (page 336, 2nd column, 2nd paragraph). The release rate of theophylline was decreased by annealing at 80oC for 4 h. Annealing of the matrix particle leads to alterations of the pellet structure and consequently, of the release properties (page 339, 1st column, 1st full paragraph). Sufficient annealing probably softens the polymer causing it to fill-in the interstices and resulting in the observed morphological changes. Thus the reduced porosity and enhanced coalescence of annealed pellets result in decreased release rates and a prolongation of the total release time (page 340, 2nd column, 1st paragraph). The theophylline release rate from annealed pellets can be controlled by varying the theophylline-to-polymer ratio and polymer properties (page 342, 2nd column, Conclusions).

Kojima et al. does not teach a matrix pellet core particles containing a pharmaceutically active substance and a matrix base material that has a hydroxyl value of 60 or greater and contains a polyglycerol fatty acid ester.

At the time of the invention, it would have been obvious to modify the method suggested by combining Akiyama et al. and Bartholomaeus et al. to include the step of annealing, i.e. heat treatment, of the granules of Kojima et al. before coating since it is a method of providing the granules with controlled release properties. Since it is an

equivalent method of preparing controlled release particles as the method of Akiyama et al. a combination of the methods would be expected to also provide controlled release granules, which is a requirement of the formulation of Akiyama et al.

All claims are rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Darryl C. Sutton whose telephone number is (571)270-3286. The examiner can normally be reached on M-Th from 7:30AM-5:00PM EST and on Fr from 7:30AM-4:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached at (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Darryl C Sutton/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612